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now available on STN
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NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
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NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 28 Oct 21 EVENTLINE has been reloaded
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NEWS EXPRESS October 14 CURRENT WINDOWS VERSION IS V6.01,
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0.21

0.21

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FILE COVERS 1907 - 30 Oct 2002 VOL 137 ISS 18

FILE LAST UPDATED: 29 Oct 2002 (20021029/ED)

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=> d 130:163108 all

ANSWER 1 CAPLUS COPYRIGHT 2002 ACS

AN 130:163108 CAPLUS

TI Diprotin A, an inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) produces naloxone-reversible analgesia in rats

AU Ronai, Andras Z.; Timar, Julianna; Mako, Eva; Erdo, Franciska; Gyarmati, Zsuzsanna; Toth, Geza; Orosz, Gyorgy; Furst, Susanne; Szekely, Jozsef I.
CS Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.

SO Life Sciences (1998), Volume Date 1999, 64(2), 145-152
CODEN: LIFSAK; ISSN: 0024-3205

PB Elsevier Science Inc.

DT Journal

LA English

CC 1-11 (Pharmacology)

Section cross-reference(s): 2

AB The dipeptidyl aminopeptidase IV (DP IV) inhibitor Diprotin A produces a full, dose-dependent, short-lasting and naloxone-reversible analgesia in the rat tail-flick test when given intracerebroventricularly, with an ED50 of 295 nmol/rat but it has no direct opioid agonist activity in the

longitudinal muscle strip of guinea-pig ileum bioassay. Two of the potential DP IV substrates, morphiceptin and endomorphin 1, identified recently in bovine brain were also analgesic given by similar route. The action of endomorphin I was more potent (ED50 = 7.9 nmol/rat) and slightly but significantly more sustained than that of Diprotin A. Diprotin A neither potentiated nor prolonged the effect of a marginally analgesic dose of endomorphin 1. The distinct time course and the lack of potentiation indicate that in the analgesic effect of Diprotin A in rats the protection of a brain Tyr-Pro-peptide other than endomorphin 1 is involved.

ST dipeptidyl aminopeptidase inhibitor Diprotin A analgesia

IT Analgesics

(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)

IT 74135-04-9, Morphiceptin 90614-48-5, Diprotin A 189388-22-5, Endomorphin 1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)

IT 54249-88-6

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Arunlakshana, O; Br J Pharmacol 1959, V14, P48 CAPLUS
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=> file reg

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FULL ESTIMATED COST

10.49

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TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Experimental and calculated property data are now available. See HELP
 PROPERTIES for more information. See STN Note 27, Searching Properties
 in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

```
=> s diprotin a
      3 DIPROTIN
      1379231 A
L1      1 DIPROTIN A
      (DIPROTIN(W)A)
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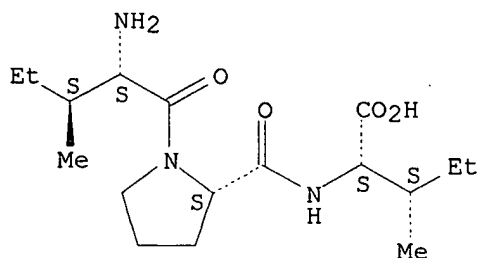
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=> d l1 all
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L1  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   90614-48-5  REGISTRY
CN   L-Isoleucine, L-isoleucyl-L-prolyl- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   L-Isoleucine, N-(1-L-isoleucyl-L-prolyl)-
OTHER NAMES:
CN   Diprotin A
FS   STEREOSEARCH
MF   C17 H31 N3 O4
CI   COM
LC   STN Files:  AGRICOLA, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS,
      CSCHM, DDFU, DRUGU, EMBASE, MEDLINE, MSDS-OHS, NAPRALERT, RTECS*,
      TOXCENTER, USPATFULL
      (*File contains numerically searchable property data)
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Ring System Data

Elemental Analysis	Elemental Sequence	Size of the Rings	Ring System Formula	Ring Identifier	RID Occurrence
EA	ES	SZ	RF	RID	Count
=====	=====	=====	=====	=====	=====
C4N	NC4	5	C4N	16.136.1	1

Absolute stereochemistry.



Calculated Properties (CALC)

CODE	PROPERTY	VALUE	CONDITION	NOTE
HD	H donors	4		(1) ACD
HAC	H acceptors	7		(1) ACD
MW	Molecular Weight	341.45		(1) ACD
LOGP	logP	1.580+/-0.656		(1) ACD
LOGD	logD	-1.52	pH 1	(1) ACD
LOGD	logD	-1.04	pH 4	(1) ACD
LOGD	logD	-0.93	pH 7	(1) ACD
LOGD	logD	-1.00	pH 8	(1) ACD
LOGD	logD	-2.10	pH 10	(1) ACD
PKA	pKa	3.68+/-0.22	Most Acidic	(1) ACD
PKA	pKa	8.64+/-0.39	Most Basic	(1) ACD
SLB.MOL	Molar Solubility	>=0.1 - <1 mol/L	pH 1	(1) ACD
SLB.MOL	Molar Solubility	>=0.1 - <1 mol/L	pH 4	(1) ACD
SLB.MOL	Molar Solubility	>=0.1 - <1 mol/L	pH 7	(1) ACD
SLB.MOL	Molar Solubility	>=0.1 - <1 mol/L	pH 8	(1) ACD
SLB.MOL	Molar Solubility	>=1 mol/L	pH 10	(1) ACD

(1) Calculated using Advanced Chemistry Development (ACD) Software Solaris V4.67 ((C) 1994-2002 ACD)

40 REFERENCES IN FILE CA (1962 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

40 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1

AN 137:68128 CA
 TI Aromatic amino acid decarboxylase proteins of a parasitic helminth, nucleic acid molecules coding them, and uses thereof
 IN Tang, Liang
 PA USA
 SO U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 129,377, abandoned.
 CODEN: USXXCO
 DT Patent
 LA English
 IC ICM A61K039-00
 ICS C07H021-04; C12N009-64; C12P021-02; C12N005-06
 NCL 424191100
 CC 63-3 (Pharmaceuticals)
 Section cross-reference(s): 1, 7, 9, 15

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002081313	A1	20020627	US 2001-777558	20010205
	WO 2000008163	A2	20000217	WO 1999-US17858	19990805
	WO 2000008163	A3	20000720		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 1998-129377		19980805		
	WO 1999-US17858		19990805		
AB	The present invention relates to parasitic helminth arom. amino acid decarboxylase proteins; to parasitic helminth arom. amino acid decarboxylase nucleic acid mols., including those that encode such arom. amino acid decarboxylase proteins; to antibodies raised against such arom. amino acid decarboxylase proteins; and to compds. that inhibit parasitic helminth arom. amino acid decarboxylase activity. The present invention also includes methods to obtain such proteins, nucleic acid mols., antibodies, and inhibitory compds. Also included in the present invention are therapeutic compns. comprising such proteins, nucleic acid mols., antibodies and/or inhibitory compds. as well as the use of such therapeutic compns. to protect animals from diseases caused by filariids. The present invention also includes a method for detecting the presence of amino acid decarboxylases.				
ST	amino acid decarboxylase				
IT	Immunostimulants (adjuvants; arom. amino acid decarboxylase proteins of a parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)				
IT	Alleles Animal tissue culture Anthelmintics Brugia malayi Dirofilaria immitis Enzyme kinetics Immunization Molecular cloning Nucleic acid hybridization PCR (polymerase chain reaction) Protein sequences Transformation, genetic cDNA sequences (arom. amino acid decarboxylase proteins of a parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)				
IT	Antibodies RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (arom. amino acid decarboxylase proteins of a parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)				
IT	Nucleic acids RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (arom. amino acid decarboxylase proteins of a parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)				
IT	Oligonucleotides RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL				

(Biological study); USES (Uses)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT Primers (nucleic acid)
 RL: PRP (Properties)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT Proteins
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT Drug delivery systems
 (carriers; arom. amino acid decarboxylase proteins of a parasitic
 helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)

IT Larva
 (filarial; arom. amino acid decarboxylase proteins of a parasitic
 helminth, nucleic acid mols. coding them, and pharmacol. uses thereof)

IT Filaria
 (larvae, molting of; arom. amino acid decarboxylase proteins of a
 parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses
 thereof)

IT Drug screening
 (of anthelmintics; arom. amino acid decarboxylase proteins of a
 parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses
 thereof)

IT Molting
 (of larval filariae; arom. amino acid decarboxylase proteins of a
 parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses
 thereof)

IT 439537-77-6 439537-81-2 439537-85-6 439537-88-9 439537-91-4
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (amino acid sequence; arom. amino acid decarboxylase proteins of a
 parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses
 thereof)

IT 9042-64-2, Aromatic amino acid decarboxylase
 RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties);
 ANST (Analytical study); BIOL (Biological study)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT 59-92-7, Dopa, biological studies 75-12-7, Formamide, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT 258873-43-7 439537-72-1 439537-73-2 439537-74-3 439537-79-8
 439537-83-4 439537-93-6
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT 51-61-6, Dopamine, formation (nonpreparative)
 RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
 (arom. amino acid decarboxylase proteins of a parasitic helminth,
 nucleic acid mols. coding them, and pharmacol. uses thereof)

IT 50-67-9, Serotonin, biological studies 53-79-2, Puromycin 55-91-4,
 Diisopropyl fluorophosphate 57-56-7, Semicarbazide 60-00-4, Edta,
 biological studies 66-71-7, 1,10-Phenanthroline 128-53-0,
 Ethylmaleimide 138-85-2 230-46-6, 1,7-Phenanthroline 329-98-6, Pmsf
 13434-13-4, Actinonin 30827-99-7, Pefabloc 36357-77-4, Phosphoramidon
 51050-59-0, 3,4-Dichloroisocoumarin 58970-76-6, Bestatin 66701-25-5,
 E-64 90614-48-5, Diprotin A 90614-49-6, Diprotin b

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)

(arom. amino acid decarboxylase proteins of a parasitic helminth,
nucleic acid mols. coding them, and pharmacol. uses thereof)

IT 439537-76-5 439537-78-7 439537-80-1 439537-82-3 439537-84-5
439537-86-7 439537-87-8 439537-89-0 439537-90-3 439537-92-5

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(nucleotide sequence; arom. amino acid decarboxylase proteins of a
parasitic helminth, nucleic acid mols. coding them, and pharmacol. uses
thereof)

REFERENCE 2

AN 137:63466 CA
TI Quantitative structure-activity relationship: IX. Estimation of logP for
some peptides
AU Golovanov, I. B.; Tsygankova, I. G.
CS Institute of Theoretical and Experimental Biophysics, Russian Academy of
Sciences, Pushchino, Russia
SO Russian Journal of General Chemistry (Translation of Zhurnal Obshchei
Khimii) (2002), 72(1), 137-143
CODEN: RJGCEK; ISSN: 1070-3632
PB MAIK Nauka/Interperiodica Publishing
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 22
AB Based on the previously described quant. structure-activity relationship,
estns. were made for the distribution factor (logP) in the octanol-water
system of amides of N-acetyl peptides and peptides contg. up to five amino
acid residues. Data for di- and tripeptides reasonably agree with the
available exptl. data.
ST peptide helical quant structure distribution factor calcn octanol water;
mol structure partition logP estn helical acetyl peptide amide
IT QSPR (structure-property relationship)
(distribution factor; quant. mol. structure-property relationship and
calcn. of distribution factor for peptides in octanol-water system)
IT Molecular structure-property relationship
(partition; quant. mol. structure-property relationship and calcn. of
distribution factor for peptides in octanol-water system)
IT Correlation analysis
Helix (conformation)
Partition
(quant. mol. structure-property relationship and calcn. of distribution
factor for peptides in octanol-water system)
IT Peptides, properties
RL: PRP (Properties)
(quant. mol. structure-property relationship and calcn. of distribution
factor for peptides in octanol-water system)
IT 74-82-8, Methane, properties 74-84-0, Ethane, properties 74-98-6,
Propane, properties 106-97-8, Butane, properties 109-66-0, Pentane,
properties 110-54-3, Hexane, properties 111-65-9, Octane, properties
111-84-2, Nonane 124-18-5, Decane 142-82-5, Heptane, properties
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 143303-37-1 143303-38-2 143303-39-3 143303-40-6 143303-41-7
 143303-42-8 143303-43-9 143303-44-0 143303-45-1 143303-46-2
 143303-47-3 143303-48-4 143303-49-5 143303-50-8 143303-51-9
 143303-52-0 143313-20-6 143313-21-7 143313-22-8 143313-23-9
 143313-24-0 143313-25-1 152971-76-1 161786-59-0 161786-60-3
 161786-66-9 161786-67-0 439809-07-1 439809-09-3

RL: PRP (Properties)

(quant. mol. structure-property relationship and calcn. of distribution
 factor for peptides in octanol-water system)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 3

AN 136:257254 CA
 TI Use of DPP IV inhibitors as diuretic and antihypertensive agents
 IN Aronson, Peter S.; Girardi, Adriana; Knauf, Felix
 PA USA
 SO U.S. Pat. Appl. Publ., 3 pp.
 CODEN: USXXCO
 DT Patent
 LA English
 IC ICM A61K031-00
 ICS C12N009-99
 NCL 514001000
 CC 1-8 (Pharmacology)
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 2002037829	A1	20020328	US 2001-938325	20010823

PRAI US 2000-227400P 20000823

AB Dipeptidyl peptidase IV inhibitors are used as diuretics and antihypertensive agents. From studies it was concluded that the DPP IV inhibitor diprotin A decreases NHE3 (Na⁺-H⁺ exchanger isoform) activity in OKP cells.

ST dipeptidyl peptidase IV inhibitor diuretic antihypertensive

IT Antihypertensives
Diuretics
(dipeptidyl peptidase IV inhibitors as diuretic and antihypertensive agents)

IT 54249-88-6, Dipeptidyl peptidase IV
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(dipeptidyl peptidase IV inhibitors as diuretic and antihypertensive agents)

IT 90614-48-5, Diprotin a
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dipeptidyl peptidase IV inhibitors as diuretic and antihypertensive agents)

REFERENCE 4

AN 135:231575 CA

TI Transbuccal peptide delivery: stability and in vitro permeation studies on endomorphin-1

AU Bird, A. P.; Faltinek, J. R.; Shojaei, A. H.

CS School of Pharmacy, Department of Pharmaceutical Sciences, Texas Tech University Health Sciences Center, Amarillo, TX, 79106, USA

SO Journal of Controlled Release (2001), 73(1), 31-36
CODEN: JCREEC; ISSN: 0168-3659

PB Elsevier Science Ireland Ltd.

DT Journal

LA English

CC 63-5 (Pharmaceuticals)

AB The purpose of this study was to investigate the feasibility of buccal delivery of a model peptide, endomorphin-1 (EN1), using stability and in vitro permeation studies. EN1 is a recently isolated .mu.-opiate receptor agonist with high selectivity and specificity for this receptor subtype. Stability studies were conducted in various buffers and the drug was shown to be stable in both acidic and basic buffer systems. In the presence of full thickness porcine buccal epithelium, EN1 was unstable with only 23.4% intact drug present after 6 h. The region responsible for this degrdn. was found to coincide with the major barrier region of the buccal epithelium as delineated through stability expts. in the presence of partial thickness buccal epithelium. Various peptidase inhibitors were used to isolate the enzyme(s) responsible for this degrdn. Diprotin-A, a potent inhibitor of dipeptidyl peptidase IV, provided inhibition of the degrdn. of EN1 in the presence of buccal epithelium. In vitro permeation studies revealed that the permeability coeff. of EN1 across porcine buccal epithelium was 5.67 .times. 10⁻⁷ cm/s. The enzymic degrdn. of EN1 was found not to be rate limiting to the drug's permeation across buccal epithelium, as diprotin-A did not increase the permeation of EN1. Na glycocholate as well as Na taurocholate were also ineffective in enhancing the permeation of EN1 across porcine buccal epithelium.

ST transbuccal peptide delivery endomorphin permeation stability

IT Drug delivery systems
(buccal; transbuccal peptide delivery)

IT Cheek
(mucosa; transbuccal peptide delivery)

IT Biological transport
(permeation; transbuccal peptide delivery)

IT Peptides, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(transbuccal peptide delivery)

IT 189388-22-5, endomorphin-1

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(transbuccal peptide delivery)

IT 90614-48-5, Diprotin-A

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(transbuccal peptide delivery, stability of endomorphin-1 in the presence of)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (19) Zadina, J; Nature 1997, V386, P499 CAPLUS

REFERENCE 5

AN 133:147118 CA

TI Relating Electrospray Ionization Response to Nonpolar Character of Small Peptides

AU Cech, Nadja B.; Enke, Christie G.

CS Department of Chemistry, University of New Mexico, Albuquerque, NM, 87131, USA

SO Analytical Chemistry (2000), 72(13), 2717-2723
CODEN: ANCHAM; ISSN: 0003-2700

PB American Chemical Society

DT Journal

LA English

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 6

AB Nonpolar regions in biol. mols. are investigated as a detg. factor governing their electrospray ionization (ESI) mass spectrometric response. Response is compared for a series of peptides whose C-terminal residue is varied among amino acids with increasingly nonpolar side chains. Increased ESI response is obsd. for peptides with more extensive nonpolar regions. The basis for this increase is examd. by comparing values of nonpolar surface area and Gibbs free energy of transfer for the different amino acid residues. Comparisons of response with octadecylamine are also made, and this highly surface-active ion is obsd. to outcompete all other analytes in ESI response. These observations are rationalized on the basis of the equil. partitioning model, which is used successfully to fit

exptl. data throughout the concn. range for several two-analyte systems. This model suggests that because excess charge exists on ESI droplet surfaces, an analyte's relative affinity for the droplet surface det. its relative ESI response. Increased nonpolar character, which leads to enhanced affinity for the surface phase, results in more successful competition for excess charge and higher ESI response.

ST small peptide electrospray ionization nonpolar character correlation
IT Electron impact ionization
Electrospray ionization mass spectrometry
Partition function
Polarity
Surface activity
(relating electrospray ionization response to nonpolar character of small peptides)
IT Peptides, properties
RL: PRP (Properties)
(relating electrospray ionization response to nonpolar character of small peptides)
IT 124-30-1, Octadecylamine 556-33-2 6234-26-0 7451-76-5 14857-82-0
17343-07-6 19729-30-7 20274-89-9 81161-89-9 90614-48-5
90614-49-6
RL: PRP (Properties)
(relating electrospray ionization response to nonpolar character of small peptides)
RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
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(20) Wolfenden, R; Biochemistry 1981, V20, P849 CAPLUS
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REFERENCE 6

AN 132:293992 CA
TI Inhibitors of Tripeptidyl Peptidase II. 2. Generation of the First Novel Lead Inhibitor of Cholecystokinin-8-Inactivating Peptidase: A Strategy for the Design of Peptidase Inhibitors
AU Ganellin, C. Robin; Bishop, Paul B.; Bambal, Ramesh B.; Chan, Suzanne M. T.; Law, James K.; Marabout, Benoit; Luthra, Pratibha Mehta; Moore, Andrew N. J.; Peschard, Olivier; Bourgeat, Pierre; Rose, Christiane; Vargas, Froylan; Schwartz, Jean-Charles
CS Department of Chemistry, University College London, London, WC1H 0AJ, UK
SO Journal of Medicinal Chemistry (2000), 43(4), 664-674
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society
DT Journal
LA English
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 7

AB The cholecystokinin-8 (CCK-8)-inactivating peptidase is a serine peptidase which has been shown to be a membrane-bound isoform of tripeptidyl peptidase II (EC 3.4.14.10). It cleaves the neurotransmitter CCK-8 sulfate at the Met-Gly bond to give Asp-Tyr(SO₃H)-Met-OH + Gly-Trp-Met-Asp-Phe-NH₂. In seeking a reversible inhibitor of this peptidase, the enzymic binding subsites were characterized using a fluorimetric assay based on the hydrolysis of the artificial substrate Ala-Ala-Phe-amidomethylcoumarin. A series of di- and tripeptides having various alkyl or aryl side chains was studied to det. the accessible vol. for binding and to probe the potential for hydrophobic interactions. From this initial study the tripeptides Ile-Pro-Ile-OH (K_i = 1 .mu.M) and Ala-Pro-Ala-OH (K_i = 3 .mu.M) and dipeptide amide Val-Nvl-NHBu (K_i = 3 .mu.M) emerged as leads. Comparison of these structures led to the synthesis of Val-Pro-NHBu (K_i = 0.57 .mu.M) which served for later optimization in the design of butabindide, a potent reversible competitive and selective inhibitor of the CCK-8-inactivating peptidase. The strategy for this work is explicitly described since it illustrates a possible general approach for peptidase inhibitor design.

ST structure activity peptide prepn inhibitor peptidase
IT Structure-activity relationship
(peptidase inhibitory; prepn. of peptides as peptidase inhibitors)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of peptides as peptidase inhibitors)

IT 1948-31-8 2390-74-1 3061-90-3 5874-90-8 6234-26-0 7349-78-2
10342-47-9 13485-59-1 13589-04-3 14486-09-0 22840-03-5
27493-61-4 53620-20-5 61430-14-6 88929-13-9 90614-48-5
121880-94-2 121880-95-3 264886-84-2 264886-88-6 264887-00-5
264887-02-7 264887-05-0 264887-06-1 264887-22-1 264887-23-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. of peptides as peptidase inhibitors)

IT 3918-92-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(prepn. of peptides as peptidase inhibitors)

IT 7530-76-9P 19542-54-2P 65849-98-1P 264887-01-6P 264887-10-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of peptides as peptidase inhibitors)

IT 3321-03-7P 3918-94-3P 82985-55-5P 264886-82-0P 264886-83-1P
264886-85-3P 264886-87-5P 264886-90-0P 264886-91-1P 264886-92-2P
264886-94-4P 264886-96-6P 264886-98-8P 264887-03-8P 264887-04-9P
264887-07-2P 264887-09-4P 264887-11-8P 264887-12-9P 264887-13-0P
264887-15-2P 264887-16-3P 264887-17-4P 264887-20-9P 264887-24-3P
264887-25-4P 264887-27-6P 264887-29-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of peptides as peptidase inhibitors)

IT 78689-82-4, Cholecystokinin-Inactivating Peptidase 101149-94-4,
Tripeptidyl Peptidase II
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(prepn. of peptides as peptidase inhibitors)

IT 64-04-0, Phenethylamine 100-52-7, Benzaldehyde, reactions 2038-57-5,
3-Phenylpropylamine 3844-54-0 13214-66-9, 4-Phenylbutylamine 39608-3
0-5 264887-32-3 264887-63-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of peptides as peptidase inhibitors)

IT 1170-76-9P 2566-19-0P 6120-70-3P 13171-93-2P 15368-72-6P
20998-83-8P 21612-32-8P 32943-08-1P 33905-01-0P 35373-92-3P
87105-26-8P 122315-77-9P 128647-50-7P 148743-43-5P 185212-81-1P
252573-92-5P 264887-54-9P 264887-55-0P 264887-56-1P 264887-57-2P
264887-58-3P 264887-59-4P 264887-60-7P 264887-61-8P 264887-62-9P
264887-64-1P 264887-65-2P 264887-66-3P 264887-67-4P 264887-68-5P
264887-69-6P 264887-70-9P 264887-71-0P 264887-72-1P 264887-73-2P
264887-74-3P 264887-75-4P 264887-76-5P 264887-77-6P 264887-78-7P
264887-79-8P 264887-80-1P 264887-81-2P 264887-82-3P 264887-83-4P
264887-84-5P 264887-85-6P 264887-86-7P 264887-88-9P 264887-89-0P
264887-90-3P 264887-91-4P 264887-92-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(prepn. of peptides as peptidase inhibitors)

IT 17136-28-6P 23361-28-6P 84717-00-0P 185212-83-3P 225386-32-3P
264886-89-7P 264887-31-2P 264887-33-4P 264887-35-6P 264887-37-8P
264887-40-3P 264887-42-5P 264887-45-8P 264887-47-0P 264887-50-5P
264887-51-6P 264887-53-8P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of peptides as peptidase inhibitors)

RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 7

- AN 131:253649 CA
- TI Aminopeptidases as potential targets for the control of the Australian sheep blowfly, *Lucilia cuprina*
- AU Reed, B. J.; Chandler, D. S.; Sandeman, R. M.
- CS Department of Agricultural Sciences, La Trobe University, Bundoora, Australia
- SO International Journal for Parasitology (1999), 29(6), 839-850
CODEN: IJPYBT; ISSN: 0020-7519
- PB Elsevier Science Ltd.
- DT Journal
- LA English
- CC 5-4 (Agrochemical Bioregulators)
- AB Expts. were carried out to investigate the role of proteinases in the growth of larvae of the sheep blowfly, *Lucilia cuprina*. First instar larvae were incubated on an artificial growth medium in the presence of various concns. of inhibitors of all the major proteinase classes. Inhibitors of serine proteinases and aminopeptidases were found to cause significant growth inhibition and in some cases death of the larvae within 24 h, suggesting that these enzymes were the major classes involved in protein digestion in the gut of the insect. A second group of expts. analyzed the effects of two inhibitors from the same or different proteinase classes in the growth media. Synergistic inhibition of larval growth was obsd. with the incorporation of inhibitors of serine proteinases and aminopeptidases. These classes of proteinases are both central to protein digestion in this insect, probably in the gut, and the inhibition of both types of activity leads to an almost complete blockade of digestion. Testing in vivo gave similar results with infections on sheep skin inhibited by either serine proteinase or aminopeptidase inhibitors and the combination of both stopped the infection process. The role of aminopeptidases in larval metab. and as potential targets for blowfly control agents is examd.
- ST *Lucilia* insecticide serine proteinase aminopeptidase inhibitors
- IT Insecticides
Lucilia cuprina
(*Lucilia cuprina* control using serine proteinase and aminopeptidase inhibitors)
- IT 60-00-4, EDTA, biological studies 2364-87-6, Tlck 9078-38-0, SBTI 13434-13-4, Actinonin 30827-99-7, Pefabloc 39324-30-6, Pepstatin 55123-66-5, Leupeptin 58970-76-6, Bestatin 62571-86-2, Captopril 67655-94-1, Amastatin 71933-13-6, APMSF 76547-98-3, Lisinopril 88264-65-7, L-Leucinthiol 90614-48-5, Diprotin A 91196-31-5, Ebelactone 110044-82-1, Calpain inhibitor I 173287-93-9 173287-94-0 173287-95-1 173287-97-3 245094-93-3 245094-97-7 245094-99-9 245095-01-6 245095-02-7 245095-03-8
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(*Lucilia cuprina* control using serine proteinase and aminopeptidase inhibitors)
- IT 9031-94-1, Aminopeptidase 37259-58-8, Serine proteinase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(Lucilia cuprina control using serine proteinase and aminopeptidase inhibitors)

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REFERENCE 8

- AN 130:163108 CA
- TI Diprotin A, an inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) produces naloxone-reversible analgesia in rats
- AU Ronai, Andras Z.; Timar, Julianna; Mako, Eva; Erdo, Franciska; Gyarmati, Zsuzsanna; Toth, Geza; Orosz, Gyorgy; Furst, Susanne; Szekely, Jozsef I.
- CS Department of Pharmacology, Semmelweis University of Medicine, Budapest, H-1445, Hung.
- SO Life Sciences (1998), Volume Date 1999, 64(2), 145-152
CODEN: LIFSAK; ISSN: 0024-3205
- PB Elsevier Science Inc.
- DT Journal
- LA English
- CC 1-11 (Pharmacology)
Section cross-reference(s): 2
- AB The dipeptidyl aminopeptidase IV (DP IV) inhibitor Diprotin A produces a full, dose-dependent, short-lasting and naloxone-reversible analgesia in the rat tail-flick test when given intracerebroventricularly, with an ED50 of 295 nmol/rat but it has no direct opioid agonist activity in the longitudinal muscle strip of guinea-pig ileum bioassay. Two of the potential DP IV substrates, morphiceptin and endomorphin 1, identified recently in bovine brain were also analgesic given by similar route. The action of endomorphin I was more potent (ED50 = 7.9 nmol/rat) and slightly but significantly more sustained than that of Diprotin A. Diprotin A neither potentiated nor prolonged the effect of a marginally analgesic dose of endomorphin 1. The distinct time course and the lack of potentiation indicate that in the analgesic effect of Diprotin A in rats the protection of a brain Tyr-Pro-peptide other than endomorphin 1 is involved.
- ST dipeptidyl aminopeptidase inhibitor Diprotin A analgesia
- IT Analgesics
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
- IT 74135-04-9, Morphiceptin 90614-48-5, Diprotin A 189388-22-5, Endomorphin 1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
- IT 54249-88-6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of dipeptidyl aminopeptidase IV(EC 3.4.14.5) Diprotin A produces naloxone-reversible analgesia in rats in relation to effect of morphiceptin and endomorphin 1)
- RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
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REFERENCE 9

- AN 129:215577 CA
- TI The significance of hypersialylation of dipeptidyl peptidase IV (CD26) in the inhibition of its activity by Tat and other cationic peptides. CD26: a subverted adhesion molecule for HIV peptide binding
- AU Smith, Robert E.; Talhouk, Jamil W.; Brown, Elvin E.; Edgar, Susan E.
- CS Prototek, Inc., Dublin, CA, 94568, USA
- SO AIDS Research and Human Retroviruses (1998), 14(10), 851-868
CODEN: ARHRE7; ISSN: 0889-2229
- PB Mary Ann Liebert, Inc.
- DT Journal
- LA English
- CC 15-8 (Immunochemistry)
Section cross-reference(s): 7
- AB The functionality of DPP-IV, purified from human placenta and isolated from CD4+/CD26+ T cells of non-infected and HIV-1-infected individuals, was investigated as to its ability to bind certain specific peptides. Using isoelec. focusing and the specificity of substrate-impregnated overlay membranes, the authors found that DPP-IV from term placenta and from T cells of HIV-infected individuals was significantly more sialylated compared with enzyme isoenzyme patterns of other tissues. The authors report here that (1) the no. of isoforms of DPP-IV and extent of sialylation are crit. to function and peptide binding; (2) the no. of sialylated isoforms isolated from PBMCs increases significantly with age greater than 40 yr; (3) hypersialylation by extreme anionic isoforms is highly assocd. with HIV infection and pathognomonic to remaining CD4+ cells in overt AIDS; and (4) highly sialylated DPP-IV is more significantly inhibited by Tat and cationic peptides. The authors conclude that hypersialylation of DPP-IV modifies surface charge of the CD26 antigen, promoting binding of HIV peptides through their cationic domains to the sialic acid residues of DPP-IV, and that certain HIV moieties are likely to engage this phenomenon as an auxiliary adhesion mechanism to fuse with cells. Furthermore, as a consequence of this occurrence, DPP-IV enzymic activity can be significantly reduced, competitively.
- ST hypersialylation dipeptidyl peptidase Tat protein; CD26 hypersialylation cationic peptide
- IT CD antigens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(CD26; hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by Tat and other cationic peptides)
- IT Peptides, biological studies
RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
(cationic; hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by Tat and other cationic peptides)

IT Envelope proteins
 RL: PRP (Properties)
 (gpl20env; hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by peptide of)

IT T cell (lymphocyte)
 (helper cell; hypersialylation of human CD26 in)

IT Aging, animal
 (hypersialylation of CD26 in human T-cells in)

IT AIDS (disease)
 Human immunodeficiency virus 1
 Sialylation
 (hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by Tat and other cationic peptides)

IT Vitronectin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by peptide of)

IT Interleukin 2 receptors
 RL: PRP (Properties)
 (hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by peptide of)

IT CD4-positive T cell
 (hypersialylation of human CD26 in)

IT Transcription factors
 RL: ADV (Adverse effect, including toxicity); PRP (Properties); BIOL (Biological study)
 (tat; hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by Tat and other cationic peptides)

IT 25104-12-5, Poly-L-ornithine 25212-18-4, Poly-L-arginine 26853-89-4, Poly-D-lysine 41961-57-3 90614-48-5 102579-44-2 151870-85-8 204570-87-6 212556-36-0 212556-37-1 212556-38-2 212556-39-3 212556-40-6
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (hypersialylation of dipeptidyl peptidase IV and inhibition of its activity by Tat and other cationic peptides)

REFERENCE 10

AN 127:326656 CA

TI Methods for the investigation of neuropeptide catabolism and stability in vitro

AU Mentlein, Rolf; Lucius, Ralph

CS Anatomisches Institut der Universitat Kiel, Kiel, D-24098, Germany

SO Brain Research Protocols (1997), 1(3), 237-246
 CODEN: BRPRFP; ISSN: 1385-299X

PB Elsevier

DT Journal

LA English

CC 2-1 (Mammalian Hormones)
 Section cross-reference(s): 9

AB The protocol describes (i) methods for the investigation of neuropeptide catabolism in the central nervous system (CNS), (ii) the identification of the neuropeptidases involved, and (iii) methods for the detn. of neuropeptide stability in vitro. These methods are applicable also to study the degrdn. of peptide hormones by peripheral cells or tissues. To identify peptide degrdn. products, nanomolar amts. (micromolar concns.) of peptides are incubated in synthetic media with cell or tissue cultures. Aliquots of the supernatants are withdrawn after different times, peptide fragments sepd. and fractionated by reversed-phase HPLC, and identified by peptide chem. methods. The peptidases responsible for this degrdn. can be

identified by the use of specific inhibitors listed in the protocol. For receptor binding assays or the study of peptide effects in physiolog., nanomolar concns. the stability of the peptides in an in vitro system should be checked by addn. of radiolabeled peptides (femtomolar or nanomolar concns.) and monitoring the peptide degradn. by a procedure analogous to that established for unlabeled peptides. The addn. of more or less specific peptidase inhibitors enhances peptide stability in vitro, and thus it can be assured that a given peptide concn. is maintained during biol. assays.

- ST neuropeptide catabolism stability neuropeptidase
- IT Metabolism
 - (catabolic; methods for investigation of neuropeptide catabolism and stability in vitro)
- IT Brain
 - (methods for investigation of neuropeptide catabolism and stability in vitro)
- IT Neuropeptides
 - RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 - (methods for investigation of neuropeptide catabolism and stability in vitro)
- IT Hormones, animal, biological studies
 - RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 - (peptide; methods for investigation of neuropeptide catabolism and stability in vitro)
- IT 9015-82-1 9031-94-1, Aminopeptidase 9031-96-3, Peptidase 9031-98-5, Carboxypeptidase 9054-63-1 9073-92-1 9074-83-3 37259-58-8, Serine protease 37353-41-6, Cysteine protease 54249-88-6 78169-47-8, Aspartic protease 81669-70-7, Metalloprotease 82707-54-8, Neprilysin 110639-28-6 148938-24-3, Meprin A 149371-24-4, Neurolysin
 - RL: ANT (Analyte); ANST (Analytical study)
 - (methods for investigation of neuropeptide catabolism and stability in vitro)
- IT 51110-01-1, Somatostatin 58822-25-6, 1-5-.beta.-Neoendorphin (human) 118549-37-4, Insulinotropin
 - RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 - (methods for investigation of neuropeptide catabolism and stability in vitro)
- IT 55-91-4, Diisopropyl fluorophosphate 66-71-7, 1,10-Phenanthroline 329-98-6, Phenylmethanesulfonyl fluoride 9087-70-1, Aprotinin 13434-13-4, Actinonin 26305-03-3 36357-77-4, Phosphoramidon 51050-59-0, 3,4-Dichloroisocoumarin 51926-51-3 58970-76-6, Bestatin 62571-86-2, Captopril 66701-25-5, E-64 67655-94-1, Amastatin 76547-98-3 76721-89-6, Thiorphan 77102-28-4 90614-48-5, Diprotin A 90614-49-6, Diprotin B 103900-19-2, Arphamenine B 116560-97-5 123652-87-9, Probestin 143983-57-7
 - RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 - (methods for investigation of neuropeptide catabolism and stability in vitro)
- IT 9001-92-7, Protease
 - RL: ANT (Analyte); ANST (Analytical study)
 - (trypsin-like; methods for investigation of neuropeptide catabolism and stability in vitro)

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Connection closed by remote host